UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MAY 5 1992

MEMORANDUM

SUBJECT: SACB Review of Toxicity Studies Submitted to Support the Registration of the End-Use Product Treo™ 3-Way Protecting Lotion (HED Project No. 2-1070; I.D. No. 065233-R; Caswell No. 618; Shaughnessy No. 021901; Barcode D173189)

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JTMC 4/29/92

THROUGH: Reto Engler, Ph.D., Chief
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ACTION REQUESTED: Primavera Laboratories, Inc. is seeking registration of an insect repellent, Treo™ 3-Way Protecting Lotion, that uses low concentrations of plant derivatives to deter ticks and biting flies. The active ingredient in Treo™ 3-Way Protecting Lotion is citronella oil. This compound is a naturally-occurring plant component which will be used at low concentrations in the lotion to repel insect pests. In response to a request by the Registration Division for an expedited review, SACB has performed a secondary review of all submitted toxicology studies and has provided a summary of the results below.

CONCLUSIONS: The toxicology studies reviewed below provide, in most instances, sufficient information to support the registration of the End-Use Product Treo™. However, certain deficiencies have been identified and are outlined below. It should be noted that SACB DID NOT review any studies where the technical grade active ingredient (TGAI) was evaluated for toxicity. Consequently, a complete battery of acute toxicity studies is required to support the registration of the TGAI (oil of citronella) in Treo™. In addition, unless specific waivers are requested by the registrant the following studies are required: Hypersensitivity Incidents (152B-16; incidents are to be reported to the Agency), Mutagenicity Assays (152B-17), and Immunotoxicity (152B-18). Based on the proposed use-pattern, SACB would expect that the primary route of

exposure would be by dermal penetration and that a 90-day Dermal (152B-21) and a Teratogenicity Study (152B-23) would be required.

STUDY SUMMARIES

152B-10. Acute Oral Toxicity. The acute oral LD_{50} for the end-use product (EP) TREO, was determined to be greater than 5 gm/kg in male and female rats. All treated animals appeared normal throughout the course of the 14-day study.

Classification: CORE Supplementary. Toxicity Category: IV. This study can be upgraded pending submission of the purity and stability of the test material and other ingredients in the EP, and individual body weights on Day 7.

152B-11. Acute Dermal Toxicity. A single application of 2000 mg/kg body weight of the test material to rabbits for a 24-hr period produced no apparent signs of treatment-related toxicity following a 14-day test period.

Classification: CORE Supplementary. Toxicity Category. III. This study can be upgraded pending submission of the purity and stability of the test material.

152B-12. Acute Inhalation Toxicity. A 4-hr exposure of the test material produced no apparent treatment-related toxicity to rats. Based on these results the LD_{50} was determined to be greater than 5.45 mg/L.

Classification: CORE Supplementary. Toxicity Category: IV. Although several deficiencies were noted, this study could be upgraded pending submission of the purity and stability of the test material and data on particle size analyses during the actual exposure period.

152B-13. Primary Eye Irritation. A single dose (0.1 ml) of the test material caused conjunctival redness in 4 of 6 rabbits at 24 hr post-application (Draize score - 2.0). At 48 hr only 1 rabbit displayed conjunctival redness (Draize score - 0.3). By 72 hr (Draize score - 0.0) all irritation was resolved.

Classification: Core Supplementary. Toxicity Category: IV. This study can be upgraded pending submission of the purity and stability of the test material and data on the ocular effects at 1 hr post-application.

152B-14. Primary Dermal Irritation. A single dose (0.5 ml) of the test material caused very slight erythema in 3 of 6 animals by 24 hr and very slight to well defined erythema in 5 of 6 animals by 72 hr. Very slight edema was noted in 1 rabbit at 24 hr and in 2 rabbits by 72 hr. Although the test material was considered a non-irritant the study should have been extended beyond the 72 hr period.

Classification: CORE Supplementary. Toxicity Category: Not applicable. This study can be upgraded pending submission of the purity and stability of the test material.

152B-15. Dermal Sensitization. Based on the data submitted the test material was not considered a skin sensitizing agent in guinea pigs.

Classification: CORE Supplementary. Toxicity Category: Not applicable. This study can be upgraded pending submission of the purity and stability of the test material and justification for eliminating the appropriate controls.

TREO - 3-WAY PROTECTING LOTION

Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PI, NOEL, LEL	TOX Category	CORE Grade/ Doc. No.
ACUTE ORAL TOX CONSUMER PROD. CORP. 90033-3 2/23/90	TREO TM SPF 15 (EP)	421513-04	LD_{50} > 5 gm/kg in rats	IV	SUPPLEMENTARY
ACUTE DERMAL U.S. TESTING COMP., INC 06301 11/19/91		421513-05	LD_{50} > 2 gm/kg in rabbits	III	SUPPLEMENTARY
ACUTE INHALATION U.S. TESTING COMPANY. 06286(-) 11/19/91		421513-06	LD_{50} > 5.45 mg/L	IV	SUPPLEMENTARY
PRIMARY EYE CONSUMER PROD. TESTING 90033-2 2/23/90		421513-07	CONJUNCTIVAL REDNESS @ 24 hr post application (2.0); @ 48 hr Draize score of 0.3; by 72 hr all irritation resolved	IV	SUPPLEMENTARY
PRIMARY DERMAL CONSUMER PROD. TEST. 90033-1 2/23/90		421513-08	slight erythema up to 72 hr; slight edema in 2 animals by 72 hr	NA	SUPPLEMENTARY
DERMAL SENSITIZATION - U.S. TESTING COMP 06362(-) 11/19/91		421513-09	NOT CONSIDERED A SKIN SENSITIZER	NA	SUPPLEMENTARY

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